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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,843	06/29/2001	James P. Beck	13615.41USU1	5924

23552 7590 03/03/2003

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EXAMINER

PATEL, SUDHAKER B

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 03/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/895,843

Applicant(s)

BECK ET AL.

Examiner

Sudhaker B. Patel, D.Sc.Tech.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-175 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☒ Claim(s) 35,98 and 109 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of: _____

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,8,11,1.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-14,22-28,36-63,99-103,110-115,122-124,128,129,132-138,146,148-150,154,155,158-166,168-172 and 174.

Continuation of Disposition of Claims: Claims rejected are 15-21,29-34,64-97,104-108,116-121,125-127,130,131,139-145,147,151-153,156,157,167,173 and 175.

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DETAILED ACTION

The claims in this application are the claims 1-175.

Applicants' communication paper # 14 dated 2/10/03 is acknowledged.

Election/Restrictions

I. Because applicants did not distinctly and specifically point out the supposed errors in the restriction/election requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Applicants have elected invention of Group IX, claims (in part) 15,16-21,29-35,64-98,104-109,116-121,125-127,130-131,139-145,147,151-153,156-157,167,173 and 175. Applicants have also elected the species of preparation 23, page 131, lines 10-11 (=N1- (1S, 2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3- (4-methyl-1-piperazinyl)propyl)-5-methyl-N3,N3-dipropylisophthalamide). Therefore, the elected species have following meanings for various variables in the generic Formula II(= (RN)-N(RN-A)-CH(R1)-CH(OH)-C(R2/R3)-(Rc-A)-N-(Z-Rc) of claim 15.

Rc-A =H;

Rc-Z =-RN-1-XN =Heterocycle with (Rc-A) N wherein 1,4-diazine i.e. piperazine is only substituted at the 2 N atoms;

RN-A =H;

RN =RN-1 -XN-;

XN- =CO;

RN-1 =RN-aryl =Phenyl optionally substituted.

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Based on above analysis, the elected species has a core: "*Me-N piperazine N-CH₂-CH(OH)-CH(-CH₂-dihalophenyl)-NH-CO-Phenyl-CO-N-dialkyl*".

Claims(in part) 15,16-21,29-35,64-98,104-109,116-121,125-127,130-131,139-145,147,151-153,156-157,167,173 and 175 read on the elected species. Claims 1-14,22-28,36-63,99-103,110-115,122-124,128-129,132-138,146,148-150,154-155,158-166,168-172,174 are withdrawn from consideration as the same constitutes non-elected subject matter 37 CFR 1.142(b).

Claims 15,16-21,29-35,64-98,104-109,116-121,125-127,130-131,139-145,147,151-153,156-157,167,173 and 175 link with other patentably distinct inventions within the parent Group IX because variables RN, R1-R3, Rc, Rc-A, and RN-A have multiples of meanings. The resulting total compounds lack a common core and are structurally diverse and patentably distinct one from the others (see rejections bellow).

Also, a reference anticipating one under 35 USC 102 would not be a reference against the others under 35 USC 103. Diverse fields of search in subclasses in classes 514,549, 552, 564, 540, 546 in the U.S. Patent classification system, and in STN/CAS search are involved.

Applicants' election of species have a **genus**: "**Rc-Z** = RN-1-XN- which with-(**Rc-A**)- N) forms a heterocycle which is 1,4- di-Nitrogen substituted piperazine; **XN** =CO; **R1** is (VI) optionally substituted benzyl , **R2 & R3 not forming a fusion** to form carbocycle or heterocycle, and the remaining variables RN, RN-A, R2 and R3 are as in claim 15. This molecule will fall in U.S. Patent Classification system in class 514, subclasses 252.12, 616, 617; class 544, subclasses 358, 398, 402.

The claims under consideration are grouped as:

Compound claims: 15-21,29-34,35.

Method of use claims: 64-97,98,104-108,109,116-121,125-127,130-131, 139-145, 151-153.

Composition and kit claims: 147, 156-157, 173,175.

Therefore, this application will be examined bearing in mind the subject matter of the elected species representing above genus. Accordingly, action on merits follows.

Priority

II. It is noted that this application appears to claim subject matter disclosed in other copending Application No. 09895871*, filed 6/29/01, and co-pending Application No.09896874 filed on 6/29/01 both of which like the instant application also claim priority from Provisional Application 60215323 filed 6/30/2000. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35

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U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Information Disclosure Statement

III. The information disclosure statement (IDS) submitted paper # 4 dated 10/22/01; paper # 8 dated 1/4/02, paper # 11 submitted 12/16/02, paper # 12 dated 1/30/03 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner for U.S.P. and foreign patents (items 1-151) which examiner could print /access from the resources available to him. Applicants are urged to provide copies of the various Journal articles listed in paper # 4 i.e. items No. 151-234 for review because the same have not been provided by the applicants together with the IDS paper(s).

Signed copies of the various IDS papers are enclosed with this communication for applicants' record.

Double Patenting

IV. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15,16-21,29-35,64-98,104-109,116-121,125-127,130-131,139-145,147,151-153,156-157,167,173 and 175 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-76 of copending Application No. 09895871. This is a provisional double patenting rejection since the conflicting

claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter.

Comparison of subject matter of claims is as follows:

R1 of ref. '871 =R1 of instant claim 15 on page 186 line 14;

R2/R3 of ref. '871 =R2 of claim 15 on page 194 line 15 and R3 of claim 15 on page 195 line 1;

RN of ref. '871 =RN of claim 15 on page 196 line 5;

Rc of ref '871 =Rc of claim 15 on page 207 line 17;

H of RN-NH- of ref. =RN-A of claim 15 on page 207 line 5;

H of Rc-NH- of ref. =Rc-A of claim 15 on page 212 line 3.

The inventor(s) and the assignee are the same for these applications.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

V. Preliminary search also revealed that there exists another independent U.S.

Application Sr. No.09896139 filed 6/29/01 and claiming priority to Provisional

Application 60252736. This application is also related to WO 2002002512. Subject

matter of claims 1-221 of ref. '139 read on to instant claims 15,16-21,29-35,64-98,104-109,116-121,125-127,130-131,139-145,147,151-153,156-157,167,173 and 175.

37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their

retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Comparison of subject matter of claims is as follows:

R1 of ref. '139 =R1 of instant claim 15 on page 186 line 14;

R2/R3 of ref. '139 =R2 of claim 15 on page 194 line 15 and R3 of claim 15 on page 195 line 1;

RN of ref.'139 =RN of claim 15 on page 196 line 5;

Rc of ref '139 =Rc of claim 15 on page 207 line 17;

H of RN-NH- of ref. =RN-A of claim 15 on page 207 line 5;

H of Rc-NH- of ref. =Rc-A of claim 15 on page 212 line 3.

VI. Preliminary search also revealed that there exists another U.S. Application Sr. No.10291318 filed 11/8/02 and claiming priority to Provisional Application 60337122. This application is also related to PCT/US 02/36072 filed 11/8/02. Subject matter of ref. "318, inventor(s) and assignee are similar to the instant application. Above mentioned applications are undergoing Preliminary Examination and are not accessible to the Examiner. Since, the subject matter and title are related to the instant application, it will be necessary to review these applications during the prosecution of this application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Claim Objections

VII. Claims 35,98,109 are objected to because of the following informalities: they are shown to be dependent on claims 1, 36, 99 respectively which are non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

VIII. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15,16-21,29-34,64-97,104-108,116-121,125-127,130-131,139-145,147,151-153,156-157,167,173 and 175 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply.

A). **Compound claims** 15-21,29-34,35 include the term: "Optionally substituted with one, two or three or four (where applicable) for alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycle, aryl ,multi-atom group, heteroaryl. It is indefinite because we are not told exactly and definitely the point of contact with the carbon atoms or heteroatoms(s) of the variables.

B). In claim 15 on page 188 line 16 recites:" pyridazinyl". It is not very clear as to what applicants want to claim. Correction is required.

C). Claims 15,-21, 29 recite:" A disubstituted amine of Formula II." A compound of Formula II" is suggested.

D). Claim 141 that is dependent on claim 140 recites the range 15 to about 1500 mg/day. Claim 140 recites 0.1 to 1000 mg/day. It is not very clear as to why applicants

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have raised the upper limit from 1000 to 1500 mg/day in claim 141, which is dependent on claim 140. Correction is required.

E). In claim 97 on page 270 line 10 recites : "succinic, succinic". Correction is required.

F). **Method of use claims** 64-97,98,104-108,109,116-121,125-127,130-131, 139-145, 151-153 recite : "treating or preventing or delay or from developing" various condition or disease. It is not very clear as to what applicants want to say exactly. Is prevention equivalent to treating or from developing or delaying? Correction(s) is required.

G). In claim 64, applicants recite: "treatment which comprises administration of a therapeutically effective amount". It is not very clear as to the step or process of administration. Correction is required.

H). In claims 139, 151 applicants recite: "comprising administering or exposing". It is not very clear as to the exact step or process of administration.

I). **Kit claims** 156, 157 recite: "comprising and at least one component". It is not very clear as to what applicants want to claim. Correction is required.

J). In claim 167 applicants recite: "one or more therapeutic agent selected from a group consisting of an antioxidant, and anti-inflammatory, a gamma secretase inhibitor, a neurotropic agent, an acetylcholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta antibody". It is indefinite because it is not very clear as to one or more, and what is the exact make up of the kit. Correction is required.

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K). **In composition claim 147** it is recited: "a composition comprising a compound and beta-secretase". It is not very clear as to make up of the composition. Correction is required.

L). In claim 175 the exact make up of a composition disposed in a cream, ointment or patch is not disclosed. Correction is required.

Therefore, it would be very difficult to practice the invention by one of ordinary skill for the various reasons stated above.

Claims 16-21,30-34,65,67-73,75-77,80-83,88,89,90,92,93,94,95,96,104-108,117-121,142-145,147,152,153, 173 are included in rejections because they are dependent on rejected claims.

IX. **RAW SEQUENCE LISTING**

Applicants' data for Raw Sequence Listing submitted on 7/13/01 is entered as paper #9.

Conclusion

Allowable Subject Matter

X. Claims 15-21,29-34,35 related to compounds would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claim 147 related to simple composition would be also consider for allowance, provided applicants resolve various issues stated earlier.

Claims 64-97 related to method of treating diseases would be also considered for allowance provided applicants resolve various issues stated earlier.

The closest prior art reference Dressman et al (WO 9509843 also cited as CAS abstract # 123:169523-1995:772556) teaches making of HIV protease inhibitor(s) (see compound on page 39 lines 9-12) with a core:

" Substituted phenol-CO-NH-CH(CH₂-S-Ph)-CH(OH)-CH₂-piperazine-CH₂-pyridine, wherein piperazine is further substituted on ring carbon atom with—CO-NH-alkyl group".

Dressman does not indicate or suggest arriving at the instant compounds.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

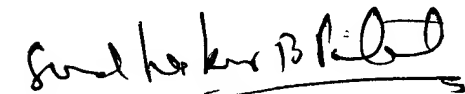
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is 703 308 4709.

The examiner can normally be reached during 6:30 to 5:00 pm on Monday-Thursday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on 703 308 4716 or Sr. Examiner Mr. Richard Raymond on 703 308 4523.

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The fax phone numbers for the organization where this application or proceeding is assigned are 703 308 4556 for regular communications and 703 308 4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.

A handwritten signature in black ink, appearing to read "Sudhaker B. Patel", with a horizontal line drawn underneath it.

Sudhaker B. Patel

March 1, 2003
